

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the claims

Claims 23-32 were previously canceled without disclaimer or prejudice thereof. Claims 40-42 are requested to be canceled without disclaimer or prejudice thereof.

Claim 10 is currently being amended to recited “wherein the inner pin has an inside diameter, and wherein the animal cell colonies being picked have a size that is smaller than the inner pin inside diameter.” The amendment adds no new matter, and exemplary support can be found throughout the specification, for example, at canceled claims 40-42 and at page 12, lines 13-16, describing one embodiment of a colony picking apparatus in which the “inner pin 64 has an inside diameter of 0.7 mm” which is “suitable for picking cell colonies of average size circa 0.5 mm.”

Applicants acknowledge that the amendment is made after a final rejection on the merits. However, because the amendment does not introduce new matter, and either place the application in condition for allowance or at least in better condition for appeal, entry and examination thereof is respectfully requested.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier. After amending the claims as set forth above, claims 1-22 and 33-39 are pending in this application.

II. Declaration of Dr. Stephen Richmond

Applicants submit herewith the declaration of Dr. Stephen Richmond, a named inventor of the present application (“the Richmond Declaration”). Applicants acknowledge that this declaration is submitted after a final rejection on the merits. Pursuant to 37 C.F.R. § 1.116 (e), Applicants respectfully assert that the declaration is necessary to overcome the pending rejections under 35 U.S.C. § 103(a); the declaration more clearly explains and clarifies distinctions between the cited art and the claimed invention. The cited art, specifically, the combination of primary references (Magnuson and Hering) was first presented in the previous, non-final Office Action dated February 3, 2009. Applicants earnestly believed that the remarks presented in the reply to this non-final Office Action would be sufficient to overcome the rejection. However, upon receipt of the final Office Action dated November 12, 2009, it was apparent that a more detailed explanation of the claimed invention and the features that distinguish it from the cited art would be necessary. Accordingly, Applicants provide the declaration of Dr. Richmond and respectfully request that the declaration be reviewed and made of record.

III. Claim rejection – 35 U.S.C. § 103(a)

Claims 1, 2, 5, 6, 10, 18-22 and 36-42 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over two primary references, U.S. Patent Publication No. 2003/0179916 to Magnuson (“Magnuson”) in view of U.S. Patent No. 6,146,881 to Hering (“Hering”). In addition, three more references are cited in conjunction with Magnuson and Hering to allegedly render obvious certain aspects of the dependent claims: U.S. Patent Publication No. 2001/0019845 to Beinert (“Beinert”), U.S. Patent No. 4,210,724 to Sogi (“Sogi”), and U.S. Patent No. 6,064,754 to Parekh (“Parekh”). Applicants respectfully traverse these grounds for rejection.

A. Magnuson and Hering

With respect to the primary references, the Office Action maintains that the combination of Magnuson and Hering renders the claimed method and apparatus obvious even though: (1) Magnuson clearly *teaches away* from the claimed invention, (2) the prophetic combination of Magnuson and Hering would not result in the claimed invention, and (3) there is no reason to modify Magnuson in light of Hering.

Relying on the Richmond Declaration, the present specification, and the teachings of the cited art, Applicants describe why the combination of Magnuson and Hering do not render the claimed invention obvious and emphasize the patentability of the claimed method and apparatus over the cited references. In addition, Applicants have amended claim 10 to further underscore the differences between the cited art and the claimed apparatus.

1. The claimed invention

The present claims are directed to a method and apparatus for picking animal cell colonies, with claims 1 and 10 being independent. Claim 1 is directed to a method for picking cell colonies. This is done by aspiration into a hollow pin. The hollow pin has an inside diameter that is greater than the size of the cell colonies to be picked. The significance of this is that an *entire colony* can be aspirated into the pin without damage. This is not taught or suggested in the cited art.

Claim 10 is directed to an apparatus for picking animal cell colonies. The apparatus includes at least one hollow pin, wherein the at least one hollow pin comprises an inner pin and an outer pin. In addition, the inner pin is recessed axially inside an end of the outer pin, and the animal cell colonies to be picked have a size that is smaller than the inside diameter of the inner pin. Like the method of claim 1, the apparatus of claim 10 allows for the aspiration of an *entire cell colony* into the inner pin without damage. Again, this is not taught or suggested in the cited art.

As attested in the accompanying Richmond Declaration, the advantages of picking an entire cell or cell colony without damage include but are not limited to the following:

(i) it is much more likely that viable cells from every clone present in the source plate will survive picking and thereby be represented in the destination plate to which they are transferred;

(ii) in the case of picking single cells, it is much less likely that a cell will be killed by the picking operation described herein, thus maintaining the complexity of the population;

(iii) attributes of the cell or cell colony will be maintained in the destination plate after picking, so that attributes already measured in the source plate before picking are maintained after picking, such as fluorescence level (which may represent productivity) and colony size (which may represent a specific cell type). This is important, since the cell or cell colony will in many cases have been selected for picking based on it having high performance in respect of one or more attributes measured in the source plate.

(iv) no cells from a picked colony will remain in the source plate, which if left behind would represent a potential contamination source for the remaining cell colonies;

(v) no cells will be deposited on the exterior of the pin in the course of picking, so that contamination of another cell colony in a subsequent picking operation is much less likely.

Richmond Declaration at ¶ 5.

2. Magnuson teaches away from the claimed invention

Magnuson is also directed to a method for picking cell colonies based on hollow-pin aspiration. However, unlike the claimed invention, Magnuson's scheme requires the hollow pin to have a diameter which is smaller than the size of the cell colonies. This requirement of Magnuson is necessary to enable the pin to form an "essentially air-tight seal" with the colony for aspiration. Magnuson at paragraph [0127].

As illustrated in Magnuson and further explained in the Richmond Declaration, Magnuson makes clear that hollow pin aspiration will not work if the picking pin diameter is greater than the colony to be picked. Furthermore, as explained in the Richmond Declaration, Magnuson demonstrates and emphasizes that to be functional, the Magnuson hollow pin aspiration method and device require that the picking tip diameter be smaller than the colony or cell to be picked.” Richmond Declaration at ¶ 14. In contrast, the claimed invention includes an inner pin with a diameter larger than a colony to be picked.

Moreover, as attested in the Declaration, a skilled and creative artisan, after having read Magnuson, would not contemplate a hollow pin aspiration scheme in which the picking tip diameter was larger than the colony or cell to be picked, because “Magnuson makes clear that such a configuration does not work.” Richmond Declaration at ¶ 14. Thus, Magnuson clearly teaches away from the claimed invention.

As stated in the M.P.E.P., “[a] *prima facie* case of obviousness may ... be rebutted by showing that the art, in any material respect, teaches away from the claimed invention.” M.P.E.P. § 2144.05.III, citations omitted.

Here, Magnuson clearly teaches away from the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

3. There is no reason or motivation to modify the aspirating pin of Magnuson pursuant to the teachings of Hering

Unlike Magnuson, Hering does not describe an automated colony picking apparatus. Richmond Declaration at ¶ 16. Rather, Hering describes “apparatuses and methods for treating or handling cells in a liquid bath” using “a ‘perfusion ring’ in sealed contact with the floor of the bath to isolate a portion of the liquid.” Richmond Declaration at ¶ 15; *see* Hering at abstract; col. 2, lines 43-45; col. 4, lines 48-51. In the Hering device, a conventional syringe or pipette (“liquid conveying device”) is used to withdraw fluid or cells from the contents inside the perfusion ring,

or to add fluid to the contents inside the perfusion ring, *see e.g.*, Hering at col. 2, lines 57-58; col. 3, lines 44-51. The syringe or pipette tip of Hering can be poked through the perfusion ring wall if the perfusion ring is made of a soft, elastic material, *see e.g.*, Hering at col. 8, lines 7-13. In addition, the syringe or pipette tip of Hering can also be inserted into a “holding member” formed on the perfusion ring. *See e.g.*, Hering at col. 2, line 57. The function of the perfusion ring is to isolate the liquid inside the perfusion ring from the rest of the bath during cell handling or treatment. *see e.g.*, Hering at col. 1, lines 5-9; Richmond Declaration at ¶ 15.

The only element of the Hering device that could reasonably be used to aspirate cells or cell colonies is the liquid conveyance device (*e.g.*, pipette tips, syringe needles).” Richmond Declaration at ¶ 17. Dr. Richmond attests that even if “[a]ssuming *arguendo* ... at least some of the liquid conveying devices described in Hering have a diameter larger than that of a cell colony (*e.g.*, pipette tips), the skilled and creative artisan would not see fit to incorporate a device with such a diameter into the automated colony picking apparatus of Magnuson” because “Magnuson clearly teaches that such a modification will not work.” Richmond Declaration at ¶ 18, emphasis added.

a. **A perfusion ring coupled to the Magnuson device will not result in the claimed method or apparatus because Magnuson teaches away from enlarging the “inner” aspirating pin**

With respect to combining the perfusion ring of Hering with the aspirating pin of Magnuson, the Examiner argues that “it would have been obvious to provide an outer hollow pin [*i.e.*, a perfusion ring] surrounding the inner hollow pin disclosed by Magnuson so that the outer hollow pin is larger than the diameter of the individual collected cell colonies.” Office Action at page 4, emphasis added. Applicants fail to see how this modification would render the claimed invention obvious.

While claim 10 recites an apparatus comprising both an inner pin and an outer pin, the inner pin diameter is recited to be larger than a colony to be picked. Thus, the combination of an

“outer pin” with a diameter larger than a colony to be picked (e.g., Hering perfusion ring) with an “inner pin” whose diameter is smaller than a colony to be picked (Magnuson aspirating pin), fails to suggest the claimed invention.

With respect to the perfusion ring, as attested to in the Declaration and disclosed in Hering, “Hering describes a perfusion ring having a diameter larger than a colony to be picked... [h]owever, the perfusion ring of Hering does not itself aspirate cells or cell colonies.” Richmond Declaration at ¶ 19, emphasis added.

Incorporation of the perfusion ring of Hering into the device of Magnuson would not provide the skilled and creative artisan with the claimed method or apparatus because the picking head of Magnuson must still be smaller than a colony to be picked. Richmond Declaration at ¶ 20. Thus, even if the skilled and creative artisan placed a Hering perfusion ring on a Magnuson aspirating pin, there would be no reason to enlarge the diameter of the Magnuson aspirating pin because such a modification is in direct contradiction to the teachings of Magnuson, as Magnuson teaches that such a device would fail to function.

The M.P.E.P. explicitly states that “[i]f a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.” M.P.E.P. § 2143.01.V, citations omitted. Accordingly, since there is no suggestion or motivation to modify the Magnuson device pursuant to the teachings of Hering, the rejection under 35 U.S.C. § 103(a) is improper, and reconsideration and withdrawal is respectfully requested.

b. A perfusion ring coupled to the Magnuson device would be redundant and detrimental

The Office Action asserts that “it would have been obvious to utilize the Hering perfusion ring when practicing the method/apparatus of Magnuson as a ‘back up’ to ensure that contamination is prevented even if the seal between inner pin tip and cell colony is

unintentionally broken at any time.” Office Action at page 12. This is not the case, and such a “back up” system would be redundant and detrimental to the Magnuson picking process.

As noted in the reply dated July 16, 2009 and in the Richmond Declaration, “the picking pin of Magnuson forms ‘an essentially airtight seal’ with the colony or cell to be picked.” Richmond Declaration at ¶ 21, citing Magnuson at paragraph [0127]. If such a seal is not formed, then “medium is aspirated instead of the colony, as described in Example 2 of Magnuson.” Richmond Declaration at ¶ 22.

With respect to the redundancy of a perfusion ring on the Magnuson device, Dr. Richmond attests that “[w]hen the required ‘essentially airtight seal’ is formed between the picking pin and the colony, there would be no need to isolate medium inside of a perfusion ring because an isolating seal is inherent in the successful Magnuson picking process.” Richmond Declaration at ¶ 21. And, in the event the picking pin of Magnuson did not form a proper seal over the colony, “[a] perfusion ring would provide no benefit with respect to aiding or ensuring colony aspiration” because “[t]he medium surrounding the colony would still be aspirated with or without a perfusion ring.” Richmond Declaration at ¶ 22.

With respect to a perfusion ring on the Magnuson device being detrimental, such a ring “would likely disrupt or smear the [chosen] colony as the picking head was moved to pick up the various portions of an entire colony.” Richmond Declaration at ¶ 23. The present methods and apparatuses would not encounter these problems because they “do not require the picking pin to form an “essentially airtight seal” with the colony to be picked and do not require the picking pin to be moved incrementally to pick an entire cell colony.” Richmond Declaration at ¶ 24.

Again, because the proposed modification would be redundant and would render the Magnuson device unsatisfactory for its intended purpose, there is no suggestion or motivation to combine the Hering perfusion ring with the colony aspirating device of Magnuson (*see* M.P.E.P. § 2143.01.V). Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

4. Other matters

The Office Action contends that one embodiment of Hering discloses “the entire outer pin (*i.e.*, perfusion ring) of Hering cover[ing]” and “envelop[ing]” “the entire cylindrical surface of the inner pin (c)”. The Office Action alleges that such a configuration is shown in Figure 5b and is described in col. 9, lines 10-15 of Hering. Office Action at page 13. With respect to this configuration, the Office Action asserts that “[s]ince cells are aspirated through the inner pin, they are also aspirated through the outer pin because the outer pin envelopes the entire body of the inner pin.” *Id.* The Office Action asserts that this embodiment of Hering is “entirely consistent with the operation of Applicants claimed invention described in Figure 7 and pages 12-13 of the instant specification.” *Id.* Applicants respectfully contend that the Examiner misconstrues Hering, and that no such embodiment is disclosed.

With respect to Hering, Figure 5B illustrates a perfusion ring which is nearly as tall as the liquid conveying device, a pipette tip (c). This is in contrast to Figure 5A which shows a perfusion ring that is considerably shorter than the liquid conveying device (pipette tip, (c)). Figures 5A and 5B are reproduced below.

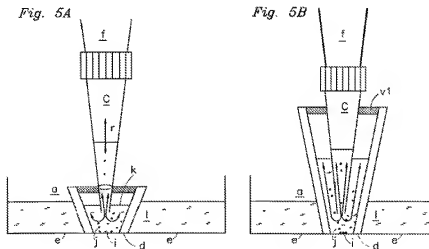


Figure 5B is described at col. 9, lines 10-15 as follows:

According to FIG. 5b, the **dimension** of the ring a is increased in order to cover the whole tip c of the pipette. The perfusion ring **forms a large volume cup** which simultaneously carries the tip c and improves the stability of the arrangement. The ring (receiving portion) and the tip can be in locked engagement.

Hering at col. 9, lines 10-15 (emphasis added).

Neither the description nor the figure imply or suggest that the perfusion ring covers/envelopes the entire cylindrical surface of the inner pin (c) as asserted in the Office Action. In fact, Figure 5B quite clearly shows that there is a space between the perfusion ring and the pipette tip, and the description clearly states that the perfusion ring “forms a large volume cup.” The description of Figure 5B states that “the dimension of the ring a is increased in order to cover the whole tip c of the pipette.” The dimension which is increased is height, and, given the fluid-filled space between the pipette tip (c) and the perfusion ring (a) shown in Figure 5B, “cover the whole tip” clearly does not mean “envelope the entire cylindrical surface” of the pipette tip as asserted in the Office Action. Moreover, in no embodiment does the perfusion ring of Hering aspirate cells or fluid. Only the “liquid conveyance device” (e.g., pipette tips) aspirate. Thus, the Examiner’s statement that “[s]ince cells are aspirated through the inner pin, they are also aspirated through the outer pin,” makes no sense and has no relevance with respect to the Hering disclosure or to the claimed invention.

Moreover, independent claim 10 specifically recites “aspirating ... into the inner pin.” Even with the Examiner’s untenable interpretation in which a perfusion ring is somehow construed as the hollow picking pin of the present claims, the claims do not recite aspiration into a perfusion ring. The function of the perfusion ring is to provide a surrounding seal, thus the colony is contained within the perfusion ring before aspiration starts. Accordingly, the Examiner’s comments regarding aspiration through a perfusion ring are not relevant to the present claims.

B. Rejection over Magnuson, Hering and Beinert

Claims 3, 13 and 33 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Magnuson and Hering as applied to claims 1 and 10, and further in view of Beinert. Office Action at page 6. Applicants respectfully traverse this ground for rejection.

The failure of Magnuson and Hering to teach or suggested the invention of claims 1, 2, 5, 6, 10, 18-22 and 36-42 is discussed above. The additional reference, Beinert, does not remedy the deficiencies of Magnuson and Hering. Beinert discloses “a freely traversable...metering head for holding, moving and releasing fluid samples, in particular a metering head having a plurality of metering devices, which can be manipulated with a picking/spotting system.” Beinert at paragraph [0012] and abstract. Beinert fails to disclose or suggest a method or apparatus for picking animal cell colonies as claimed in the present application.

Therefore, claims 3, 13 and 33 are patentable under 35 U.S.C. § 103(a) over the combination of Magnuson, Hering and Beinert, and reconsideration and withdrawal of the rejection is respectfully requested.

C. Rejection over Magnuson, Hering and Sogi

Claims 4, 11, 12, 34 and 35 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Magnuson and Hering as applied to claims 1 and 10, and further in view of Sogi. Office Action at page 7. Applicants respectfully traverse this ground for rejection.

The failure of Magnuson and Hering to teach or suggested the invention of claims 1, 2, 5, 6, 10, 18-22 and 36-42 is discussed above. The additional reference, Sogi, does not remedy the deficiencies of Magnuson and Hering. Sogi is directed to an apparatus for use in an automatic culture system, for liquid disposal and distribution, and for transferring cells being cultured from a culture vessel into a centrifuge and vice versa. Sogi at col. 1, lines 7-14. Sogi fails to disclose or suggest a method or apparatus for picking animal cell colonies as claimed in the present application. Therefore, claims 4, 11, 12, 34 and 35 are patentable under 35 U.S.C. § 103(a) over

the combination of Magnuson, Hering and Sogi, and reconsideration and withdrawal of the rejection is respectfully requested.

D. Rejection over Magnuson, Hering and Parekh

Claims 4, 7-9, 11, 12 and 14-17 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Magnuson and Hering as applied to claims 1 and 10, and further in view of Parekh. Office Action at page 8. Applicants respectfully traverse this ground for rejection.

The failure of Magnuson and Hering to teach or suggested the invention of claims 1, 2, 5, 6, 10, 18-22 and 36-42 is discussed above. The additional reference, Parekh, does not remedy the deficiencies of Magnuson and Haring. Parekh is drawn to “computer-assisted methods and apparatus for identifying, selecting and characterizing biomolecules in a biological sample.” Parekh at abstract. However, Parekh fails to disclose or suggest a method or apparatus for picking animal cell colonies as claimed in the present application. Therefore, claims 4, 7-9, 11, 12 and 14-17 are patentable under 35 U.S.C. § 103(a) over the combination of Magnuson, Hering and Parekh, and reconsideration and withdrawal of the rejection is respectfully requested.

IV. Conclusion

The present application is now in condition for allowance. Favorable reconsideration of the application is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to

Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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